



REMARKS

The present invention relates to an apparatus for isolating biomolecules. Claims 1-29 are pending in the application. Claims 1-9 and 25-29 stand rejected, while claims 10-24 have been withdrawn by the response to the Restriction Requirement filed March 16, 2005.

Rejection of claims 1-9 pursuant to 35 U.S.C. §112, first paragraph

Claims 1-9 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In particular, according to the Patent Office (the Office) the specification does not enable one skilled in the art to make a capture device having a specific "half life of binding" or a specific "half life of release." According to the Office, the definitions of "half life of binding" or a specific "half life of release" do not appear to take into account any reaction rate constants or the initial concentration of maleic anhydride or initial concentration of biomolecules. According to Lodish et al, the rate of a chemical reaction is affected by the initial concentration of reactants as well as the forward and reverse rate constants.

Applicant respectfully submits that because the present invention is a unimolecular reaction, one of skill in the art can readily make a capture device of the presently claimed invention without necessarily having in hand reaction rate constants or the initial concentration of maleic anhydride or the initial concentration of biomolecules. More simply, because the state of the prior art does in fact recognize the concepts of half life of binding and release in unimolecular reactions, one of skill in the art would be apprised of the definition and protocol for their determination, as hereafter detailed.

In the present invention, reactant biomolecules rearrange to a single product molecule. More specifically, at a first pH the biomolecules reversibly covalently bind to the binding compounds. No interaction with other molecules occurs while this step is taking place. Similarly, at a second pH, biomolecules are released from the binding compounds. Therefore, the reaction rate constants or the initial concentration of maleic anhydride or initial concentration of biomolecules is irrelevant, and as described below any experimentation to determine the parameters of the invention are not undue.

Specifically, the amount of unbound biomolecules present, during either the binding phase (a first pH) or release phase (a second pH), can be easily empirically measured using well established techniques apparent to one of skill in the art, e.g., an assay. Accordingly, using the techniques such as an assay, one of skill in the art can very easily determine, with little

experimentation using well established techniques, the time duration for half of the biomolecules to bind to (at a first pH) or release from (at a second pH) the apparatus of the presently claimed invention. Therefore, applicants assert that any experimentation that is necessary to determine the parameters of the present invention is *not* undue, but rather simple and straightforward.

Applicants also respectfully point out that the general concept of “half-life” is shown and described in the cited Shetty et al. reference, entitled “Ready separation of proteins from nucleoprotein complexes by reversible modification of lysine residues.” In particular, applicant points the Examiner’s attention to Fig. 2. Applicants note that there, the scientists described that about 50% (i.e., half) of the citraconylated protein was deacylated after about 1 hour (at a pH between 3 to 5). Further, on page 271 of the same article, the times for deacylation of citraconyl groups was determined. Applicant asserts that the principles described in the Shetty et al. reference are also applicable (without undue modification) to the present invention and that one of skill in the art, using well established techniques, can determine the parameters of the invention without undue experimentation.

Accordingly, applicant respectfully request withdrawal of the rejection to claims 1-9 under 35 U.S.C. § 112, first paragraph.

Rejection of claims 1-9 pursuant to 35 U.S.C. §112, second paragraph

Claims 1-9 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Office, with respect to claim 1, it is not clear how one skilled in the art can make a capture device having a specific half life of binding or release and does not take into account initial concentration of reactants as well as forward and reverse rate constants.

As detailed above, the initial concentration of reactants as well as forward and reverse rate constants are not relevant for determining the parameters of the present invention because the present invention is a unimolecular reaction. Because one of skill in the art can easily determine the specific half life of binding or release for a device of the present invention, using well established techniques, the rejection is improper and applicant respectfully requests its withdrawal.

Additionally, claim 1 stands rejected because the Office is not sure whether/how “biomolecules” are incorporated into the claimed device. Applicant asserts that with respect to the claim, a reference to a biomolecule is necessary to determine a half life of either binding or

release. In other words, without biomolecules to bind and release, half lives of binding and release over a time interval would be meaningless because there would be nothing to bind or release over a period of time. Accordingly, applicant respectfully requests withdrawal of the rejection. Similarly, the rejection of claim 8 with respect to antecedent basis of the term “biomolecule” should also be withdrawn as the term is a part of claim 1 and therefore antecedent basis is proper.

Claims 1 and 25 stand rejected because according to the Office, the recitation of “a maleic anhydride biomolecule-binding compound” is grammatically awkward. Applicants assert that the phrase is not grammatically awkward and that the phrase means precisely what it says, namely a single entity “maleic anhydride biomolecule-binding compound,” or in other words a maleic anhydride compound that binds biomolecules. Accordingly, applicant respectfully requests withdrawal of the rejection.

Similarly, applicants respectfully request withdrawal of the rejection of claims 1 and 25 in light of the hyphen between terms. As stated above, the claim recites a single entity “maleic anhydride biomolecule-binding compound.”

Claims 8 and 9 stand rejected as grammatically awkward and indefinite for the recitation of “amine containing compound.” The phrase means what it says, namely an “amine containing compound” or in less concise words a “compound that contains an amine.” Accordingly, applicant respectfully requests withdrawal of the rejection.

Rejection of claims pursuant to 35 U.S.C. §102(b)

Claims 1-4 and 7-9 stand rejected under 35 U.S.C. § 102(b) as anticipated by Singh et al. According to the Office, Singh describes a maleic anhydride biomolecule-binding compound covalently bound to a surface. Applicant respectfully disagrees for the reasons set forth below.

The compound disclosed in Singh et al. is not maleic anhydride but rather a maleimido group which is attached to agarose via a cleavable phenyl ester linkage. The maleimido group can be made by reacting maleic anhydride and a monohydrochloride, as described in the Materials and Methods section of Singh et al. In no case does Singh disclose or suggest a support with maleic anhydride attached thereto. Accordingly, applicant respectfully requests withdrawal of the rejection.

Similarly, because Singh et al. does not disclose a maleic anhydride attached to a support, applicant also requests that the rejection of claims 2-4, 7, 8-9, 26, and 28-29 be withdrawn.

Rejection of claims pursuant to 35 U.S.C. §102(e)

Claims 1-3, 5-9, 25, and 27-29 stand rejected under 35 U.S.C. § 102 (e) as being anticipated by Johnson et al., U.S. Patent No. 6,372,813. According to the Office, Johnson et al. discloses a biomolecule capture device comprising a maleic anhydride biomolecule-binding compound. Applicant respectfully disagrees for the reasons set forth below.

Specifically, Johnson et al. merely discloses a citraconic compound, and not a maleic anhydride compound. Specifically, the compound disclosed in Johnson et al. includes a nitrogen in the ring structure of the disclosed compound whereas the claimed maleic anhydride includes an oxygen, as shown in Fig. 1 of the present application. Accordingly, because the compound are distinct from each other, applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 102 (e).

Similarly, because Johnsons et al. does not disclose a maleic anhydride compound, the rejection of claims 2-3, 5-6, 8-9, 25, 27, 28-29 should also be withdrawn.

Rejection of claims pursuant to 35 U.S.C. §103

Claims 5-6 and 25-29 stand rejected under 35 U.S.C. § 103 as unpatentable over Singh et al. in view in Kinsella et al., U.S. Patent No. 4,348,479.

As indicated above, Singh et al. does not disclose a maleic anhydride, much less a dialkyl maleic anhydride, bound to a support. Accordingly, even if combined the combination would not result in the claimed invention of a maleic anhydride bound to a support.

However, even if Singh et al. were a relevant 35 U.S.C. 102 reference for combination with Kinsella et al, applicant respectfully submits that Kinsella et al. teaches away from such a combination. As shown at column 4, lines 20 to 30, Kinsella et al. indicates that it is **essential that the anhydride be added** to the cell homogenate incrementally, such that the pH can be monitored and to thereafter gather a precipitate. Therefore, Kinsella et al. teaches away from a combination of an anhydride with a solid support because Kinsella et al. requires that the anhydride be in a solution to be incrementally added to the homogenate, and accordingly, the rejection is improper under § 103. Accordingly, applicant respectfully requests withdrawal of the rejection.

Summary

Applicants respectfully submit that each rejection of the Examiner to the claims of the present application has been overcome, and that claims 1-9 and 25-29 are now in condition for allowance. Applicants further submit that no new matter has been added by way of the present amendment. Reconsideration and allowance of these claims is respectfully requested at the earliest possible date.

Respectfully submitted,

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